ADVISORY COMMITTEE FOR ENERGY-RELATED EPIDEMIOLOGIC RESEARCH

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APR 18 2001

Mr. Barry Fountos
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Germantown, Maryland 20874

Dear Mr. Fountos:

Enclosed is a copy of the final report, *Management and Scientific Review of the National Cancer Institute's Chernobyl Studies*, prepared by the Subcommittee for Management Review of the Chernobyl Studies (SMRCS) of the Department of Health and Human Services' Advisory Committee for Energy-Related Epidemiologic Research (ACERER).

This report was submitted to the Office of Science Policy, Department of Health and Human Services (HHS), on August 11, 2000, underwent a detailed review by various HHS staff, and was recently submitted by HHS to Congress.

The successful completion of this report was made possible by the assistance and information provided by numerous individuals currently or previously involved with the studies. We thank you for your willingness to participate in this important work.

Sincerely,

John R. Bagby
Chair, ACERER

Genevieve M. Matanoski, M.D., Dr.P.H.
Chair, SMRCS

Michael J. Sage
Executive Secretary, ACERER

Enclosure

REPORT TO

THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

MANAGEMENT AND SCIENTIFIC REVIEW OF THE NATIONAL CANCER INSTITUTE'S CHERNOBYL STUDIES

PREPARED BY:

THE SUBCOMMITTEE FOR MANAGEMENT REVIEW
OF THE CHERNOBYL STUDIES OF THE
ADVISORY COMMITTEE FOR
ENERGY-RELATED EPIDEMIOLOGIC RESEARCH

August 11, 2000

EXECUTIVE SUMMARY

Introduction

In September 1998, the Permanent Subcommittee on Investigations of the Committee on Government Affairs in the United States (U.S.) Senate held a hearing on the National Cancer Institute's (NCI) management of its radiation studies. The hearing was prompted by NCI's delays in releasing its study of potential radiation exposures to persons in the U.S. from nuclear weapons testing, but the agency's Chernobyl health effects studies were also reviewed. The Subcommittee concluded that the Chernobyl studies were delayed, lacked sufficient management oversight, and lacked measures to ensure openness and sharing of information with Federal entities and the public. As a result, the Subcommittee recommended that the Department of Health and Human Services (HHS) arrange an independent scientific and management review of the NCI Chernobyl studies. HHS agreed to carry out this recommendation.

In April 1999, HHS requested that its Advisory Committee for Energy-Related Epidemiologic Research (ACERER) conduct the review. ACERER is a Federally-chartered committee with a membership of non-Federal experts in radiation health effects and dosimetry, epidemiology, and public health. Representatives from affected communities and worker populations serve on the committee as well. ACERER accepted the task and its Chairman appointed four ACERER members to a Subcommittee for Management Review of the Chernobyl Studies (SMRCS) to conduct the review.

SMRCS began this undertaking by reviewing a voluminous amount of historical and contemporary documents associated with the study. Interviews were conducted with both former and current scientists and managers with key roles in the study including scientists from Ukraine (UA) and Belarus (BY). In April 2000, SMRCS also conducted site visits to UA and BY to review screening, clinical, dosimetry, data management, and other operations associated with the studies. To provide a forum for input and to share information about its activities, SMRCS held four public meetings attended by representatives from HHS, NCI, the U.S. Department of Energy (DOE), and public interest groups.

The primary focus of this review has been the thyroid studies being carried out with UA and BY. The NCI leukemia study with UA is an occupational study of post-accident workers and the study's feasibility component was not completed until recently. Additionally, the primary focus of the Hearing was the thyroid disease studies.

A review of the background and history of these studies was necessary to develop information to address questions presented to ACERER by HHS and to place current NCI efforts into an historical context. However, SMRCS believes that among its primary contributions are recommendations that can help NCI and its collaborators ensure the ultimate success of these studies.

Background

On April 26, 1986, a nuclear reactor at the Chernobyl nuclear power plant exploded. Millions of curies of iodine-131 (I-131) and other radionuclides were released into the atmosphere and caused millions of people to be exposed. The heaviest exposures were to the UA and BY populations. Thousands of workers (or "liquidators") were also exposed to high radiation levels while subduing fires, and stabilizing and cleaning up the site.

Authorities in the Union of Soviet Socialist Republics (USSR) initially refused to accept assistance from the U.S. and other countries. In 1988, however, the U.S. Nuclear Regulatory Commission (acting on behalf of the U.S. Government) and the USSR signed a Memorandum of Cooperation (MOC) that covered general civilian nuclear reactor health effects, safety, and environmental protection issues. The MOC did not address these issues in the specific context of the Chernobyl accident, but the framework and mechanism that led to eventual U.S. involvement in Chernobyl health effects research in UA and BY were established.

Agencies and organizations in the U.S. and throughout the world expressed an interest in providing humanitarian assistance to the people of the USSR and addressing important research questions afforded by the Chernobyl tragedy. Many U.S. researchers were interested in the effects of varying I-131 exposures to children and the subsequent development of thyroid disease (including thyroid cancer), and the relationship between exposure to ionizing radiation and the development of leukemia among clean-up workers. The potential public health relevance of such studies is that UA and BY health authorities could better plan for disease burdens that could occur in their populations over time, and to help in the development of a public health preparedness and response plan should a similar event occur elsewhere in the world.

Under the MOC, Working Group 7 was established under DOE's direction to address Chernobyl-related health and scientific issues; several NCI staff members served as experts on this Working Group. In 1990, the Working Group members met with USSR authorities to begin discussions on the need to conduct epidemiologic studies related to thyroid disease among children and leukemia among liquidators. During the discussions

and other concurrent site visits by NCI staff and others, several difficulties were identified which could arise from studies implemented collaboratively by U.S. and USSR scientists. These included USSR's position that addressing the health care needs of its radiation-exposed citizens had higher priority than research; inconsistent levels of training among USSR scientists, particularly in chronic disease epidemiology; outdated computer and medical equipment; barriers to U.S. scientists to fully access data and to ensure data would be made available for independent analyses; and recruitment and long-term retention of study populations.

In 1990, DOE requested that NCI determine the feasibility of implementing the studies. To formalize the request, Interagency Agreements (IAG) between DOE and NCI were developed, but the documents were written in general terms and gave NCI significant latitude and responsibility. For example, time lines and deliverables were not specified and the roles and responsibilities of the two agencies were not outlined until December 1996. Over time, this lack of specificity led to misunderstandings between the agencies, particularly as time passed and new senior staff at DOE replaced those who originally executed these early IAGs.

NCI was hampered in its work because of obstacles in addition to those noted above. The breakup of USSR in 1991 caused political and economic uncertainties, and existing agreements and understandings between NCI and USSR had to be renegotiated with the newly independent countries of UA and BY. Relatedly, study leadership and scientific staff in the Health Ministries of both countries frequently changed during the next several years. In addition, through the efforts of a leading Lawrence Livermore National Laboratory (LLNL) dosimetrist who had been a scientific collaborator on these studies from the outset, LLNL agreed to provide support to the studies by purchasing and delivering needed supplies and equipment to USSR and later to UA and BY. Despite many obstacles, including complex taxation and customs barriers in UA and BY, required supplies and equipment were successfully obtained and delivered to these two countries. This successful effort was led by LLNL's Ms. Sheilah Hendrickson. Complications and delays arose, for example, when the studies were unable to be launched when expected and some medical supplies became outdated. In 1996, NCI negotiated an agreement with the Veterans Affairs National Acquisition Center to become its procurement agent, but this proved to be an unsatisfactory long-term solution. It was not until April 1999, when NCI's contract with Columbia University was expanded to include providing logistics support to the studies, that this procurement function was fully re-established.

By 1996, scientific protocols for the thyroid and leukemia studies were developed by NCI, DOE, the agencies' collaborators, and by UA and BY scientists. Additionally,

Institutional Review Boards (IRBs) were established in UA and BY, and the thyroid disease and leukemia protocols were approved by the NCI IRB and by the National Institutes of Health Office for Protection from Research Risks. However, by early 1996, relationships between NCI and DOE and some other partners became contentious enough that they led to the involvement of senior DOE and NCI staff. Subsequently, in December 1996, a new IAG was signed between DOE and NCI that clearly delineated the roles of each agency. NCI would assume responsibility for all management and scientific aspects of the study; would secure contractors to support NCI scientists; and would comply with DOE financial and programmatic reporting requirements. NCI and DOE continue to comply with the terms of this IAG.

NCI has implemented the following measures to substantially strengthen the science and management of the Chernobyl studies.

1. In 1997, NCI awarded a contract to Columbia University to assume many scientific, administrative, and logistical responsibilities. The contract, that encompasses both the leukemia and thyroid disease studies, is being conducted under the leadership of Columbia's Dr. Geoffrey Howe, an internationally respected radiation epidemiologist. A multi-disciplinary team of leading scientists has been assembled by Dr. Howe to assist him in this effort.

2. In 1999, NCI transferred the Chernobyl Research Program from the Division of Cancer Biology to the Division of Cancer Epidemiology and Genetics (DCEG) to strengthen scientific oversight. Under the direction of Dr. Gilbert Beebe, a Chernobyl Research Unit was formed in the DCEG, Radiation Epidemiology Branch (REB). Dr. Elaine Ron serves as the Branch Chief and Dr. Ihor Masnyk was appointed Project Director of the studies. Additional staff were hired to strengthen NCI's Chernobyl studies program. Procedures were implemented to improve program oversight and accountability with NCI leadership, DOE, and others.

FINDINGS

1. Nonspecific IAGs between NCI and its collaborators, particularly DOE, led to misunderstandings which adversely affected the implementation of the studies in the initial years of operation.

2. The breakup of USSR led to delays in fully implementing these studies.

3. NCI launched the studies with only three scientists. The project was insufficiently staffed to effectively fulfill a mission of this magnitude with respect to its complexity, scientific merit, and political importance. No written evidence indicates that the scientists regularly informed senior NCI management about the serious problems that developed or sought assistance in this regard. Conversely, senior NCI management did not appear to make significant efforts to learn about the direction and progress of the studies. The lack of public participation in and independent scientific peer review of the studies materially contributed to these problems.

4. The reorganization of the studies within NCI and the Columbia University contract have substantially strengthened accountability and have enhanced the studies from both scientific and management perspectives. UA and BY Health Ministries and staff scientists appear to be committed to conducting the studies. UA and BY staff scientists are becoming increasingly skilled in carrying out their scientific responsibilities. Current management and study implementation procedures have improved and demonstrate excellent potential for success if remaining issues are resolved. The potential scientific and public health value of the studies is significant, and they should be continued under NCI's leadership.

5. NCI scientists took steps to avoid overlap with other research groups conducting Chernobyl-related studies in UA and BY and related scientific information was shared among these groups in various scientific forums; however, with the exception of the dosimetry component of the NCI studies, there was no apparent effort on NCI's part to take advantage of collaborative opportunities that may have existed with these parties.

6. Many committed scientists and managers from NCI, DOE, LLNL, and academia worked on the studies for many years and under challenging circumstances. An important legacy of their work is a well-equipped and trained cadre of research and medical personnel in UA and BY. NCI, Columbia University, and others are continuing the process of strengthening this model. This alone will benefit UA and BY citizens long-term.

RECOMMENDATIONS

While substantial progress has been made with regard to strengthening the scientific and management aspects of these studies, several significant problems must be addressed and promptly resolved to ensure the successful outcome of these studies.

1. While the thyroid disease study design is appropriate, the scientific feasibility of the studies has remaining problems and challenges. Most prominent among them are locating an adequate number of study subjects (up to 12,000 people each in UA and BY for the thyroid studies) and retaining them in the studies over the 10 or more remaining years of the studies, and minimizing study bias issues described in the full report. Methodologies for including uncertainty and sensitivity analyses in these studies needs to be addressed. Additionally, NCI needs to work with UA and BY authorities to ensure that NCI and Columbia University researchers have full and complete access to all study-generated data, with the optimum situation being to ensure these data become available for independent analyses.

2. The feasibility of the project, adherence to goals, and appropriate management needs to be assessed on an ongoing basis by a peer review group independent of NCI and its contractors. This group should include all scientific disciplines involved in the project, should be comprised of individuals who have not had involvement in the studies from their inception, should include liaison members from its Bi-National Review Group, and should include a public input component The public input component should include representatives of relevant public interest groups as well as concerned citizens.

3. The scientific protocols for the thyroid studies need to be revised, peer reviewed, and updated and should include detailed descriptions of study goals; specific and measurable objectives and methods; clearly delineated time-lines; and publication and communication plans. These components need to evaluated and regularly re-evaluated over the life of the studies. The protocols should also recognize the need to develop a plan to address long-range public health implications of study results and the need to develop a guidance document for public health planning and response for similar disasters that may occur elsewhere. The protocols should be broadly disseminated to ensure openness and accountability as the studies continue.

4. Columbia University and UA staff have developed creative outreach and health education programs to inform UA citizens about the importance of the UA thyroid

study. These programs as well as modest cash incentives to help defray individuals' costs for participating in the studies are increasing recruitment and public participation, particularly in rural areas. These efforts should be strengthened in UA and similar strategies must be encouraged in BY. NCI or Columbia University should consider employing a health education specialist to enhance this critical component of the studies.

5. UA and BY scientists and staff are commended in conducting their responsibilities under extremely challenging physical and logistical conditions. Substantial progress has been made to ensure that financial support, supplies, and equipment to UA and BY are promptly delivered, but problems still remain. NCI and Columbia University need to ensure that required resources are provided to UA and BY scientists when needed.

6. NCI is encouraged to proceed with its plan to conduct a meeting of other U.S. and international Chernobyl researchers to share information and to identify potential collaborative opportunities. Additionally, its successful November 1999 meeting of NCI, Columbia University, UA, and BY scientists for the first time brought all scientists participating in NCI-sponsored thyroid disease studies into one forum. Such meetings should be replicated on a periodic basis and be open to the public and other scientists who may wish to attend.

REPORT TO
THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

MANAGEMENT AND SCIENTIFIC REVIEW OF THE NATIONAL CANCER INSTITUTE'S CHERNOBYL STUDIES

Background and Purpose[1]

On September 16, 1998, the Permanent Subcommittee on Investigations of the Committee on Governmental Affairs in the United States (U.S.) Senate held a hearing on the National Cancer Institute's (NCI) management of its radiation studies. The Subcommittee focused much of its attention on NCI's assessment of potential radiation exposures to persons in the U.S. from above-ground nuclear weapons testing conducted by the Government during the 1950s. The Subcommittee was concerned that NCI completed the study after 14 years and released the findings in October 1997 only after pressure from Congress and public interest groups. Concerns were also raised that the NCI report did not include public health information about the risk of cancer associated with these radiation exposures. The Subcommittee attempted to determine the cause of the delay in order to prevent these problems from affecting other studies managed by NCI. As a result, the Subcommittee also reviewed NCI's Chernobyl [2] health effects studies.

The Subcommittee concluded that the Chernobyl studies were inordinately delayed, lacked appropriate management oversight and standards, and had no existing measures to ensure openness and full disclosure of information to the public and State and Federal agencies. In particular, the Subcommittee recommended that "HHS institute an independent management review and scientific audit of the Chernobyl projects to identify

[1]Note that the primary focus of this review has been the thyroid disease studies being carried out with Ukraine and Belarus. The NCI leukemia study with Ukraine is an occupational study of post-accident workers and the study's Phase I feasibility component was not completed until recently. Additionally, the primary focus of the Hearing was the thyroid disease studies. NCI has recently developed a revised draft leukemia protocol with more limited scientific objectives than were envisioned in its original, 1996 leukemia protocol. In part this is because of the difficulty of establishing individual radiation doses for exposed workers. The development of the revised protocol is being carried out with external scientific guidance and review and study stopping rules are under development to help prevent the study from continuing in the face of insurmountable obstacles. Columbia University, NCI's scientific and logistics contractor for the thyroid studies, also will continue to work in conjunction with NCI in the conduct of the leukemia study.

[2]The current and preferred spelling is "Chornobyl"; however, "Chernobyl" will be used in this report to be consistent with historical literature.

the areas that warrant improvement in order to increase the chances of successful completion of the studies." The Department of Health and Human Services (HHS) responded by committing to ". . . work with NCI staff to arrange for an independent review of the Chernobyl project to identify any problems associated with the way the work is planned, organized, conducted, and overseen." The Subcommittee's recommendation for this review was formalized in the fiscal year (FY) 1999 Department of Labor, Health and Human Services, and Education Appropriations Conference Report.

In April 1999, HHS proposed that its Advisory Committee for Energy-Related Epidemiologic Research (ACERER)[3] perform the review. In May 1999, ACERER accepted the task and its Chairman appointed four ACERER members to the Subcommittee for Management Review of the Chernobyl Studies (SMRCS) to conduct the review. (SMRCS members, Attachment II)

The broad focus of the SMRCS review has been on identifying challenges and opportunities faced by Ukrainian and Belarussian scientists, as well as NCI scientists, contractors and collaborators in implementing the studies; determining the type and amount of input and involvement from Ukraine (UA) and Belarus (BY) local leaders and the public in the studies; and characterizing the nature and extent of the collaboration among scientists in the U.S., UA, and BY. SMRCS also assessed NCI's conduct of the studies consistent with questions HHS developed for this review.

A review of the background and history of these studies was necessary to develop information to address questions presented to ACERER by HHS and to place current NCI efforts into an historical context. However, SMRCS believes that among its primary contributions are recommendations that can help NCI and its collaborators ensure the ultimate success of these studies.

[3]ACERER is a Federally-chartered advisory committee charged with providing guidance and recommendations to the Secretary, HHS, the Director of the Centers for Disease Control and Prevention, and the Administrator of the Agency for Toxic Substances and Disease Registry. ACERER advises HHS on the establishment of research agendas and the conduct of research programs pertaining to energy-related (primarily radiation-related) epidemiologic studies. ACERER's membership is non-Federal experts in radiation health effects, radiation dosimetry, epidemiologic research and public health. Representatives from public interest groups, affected communities, and worker populations serve on the Committee as well. (See Attachment I for the current ACERER membership roster.)

Review Methods

SMRCS and support staff began this undertaking by reviewing a voluminous amount of historical and contemporary scientific and management documents collected during the studies. The materials included all documentation provided by NCI to the Permanent Subcommittee on Investigations: site visit reports prepared by NCI, the Department of Energy (DOE), Columbia University staff, and other collaborators; internal memoranda; correspondence to and from external parties; financial data; scientific protocols, proposals, and reports; and formal agreements between NCI and other Federal agencies. SMRCS interviewed NCI and other Government scientists who were or are currently involved in the studies, other Federal officials, Columbia University scientists, as well as UA and BY Project Directors and senior and staff scientists. (Interviewees, Attachment III)

On April 11-20, 2000, a SMRCS-led team also conducted site visits to the UA and BY projects to review the scientists' screening, clinical, data management, dosimetry, and other operations associated with the studies.

To provide a forum for input and share information about these activities, SMRCS (1) held four public meetings with representatives from HHS, DOE, NCI, and public interest groups; (2) briefed ACERER and its Subcommittee for Community Affairs (SCA) on the progress to date on December 16, 1999; (3) presented its draft findings to the HHS Deputy Assistant Secretary, Office of Science Policy, on May 26, 2000; and (4) presented the preliminary conclusions to NCI, DOE, and the Department of State (DOS) on June 1, 2000. At each briefing, SMRCS emphasized that recommendations and other components of the final report could change based on ACERER's comments. Draft copies of the report were not provided to HHS, NCI, DOE, or DOS at these briefings. The draft report was sent to ACERER members on June 1, 2000, and the draft report's major findings and recommendations were presented by the SMRCS Chairperson to ACERER membership and ACERER/SCA consultants at the June 7, 2000, ACERER meeting. ACERER members' comments were considered by SMRCS for inclusion in the final report. This report was unanimously approved by a quorum of ACERER members on August 4, 2000. (Attachment IV, SMRCS Time Line and Review of Major Events).

History of Early U.S. Government Involvement in Chernobyl Issues

On April 26, 1986, a nuclear reactor at the Chernobyl nuclear power plant complex exploded. Approximately 40-50 million curies of iodine-131 (I-131) and other radioiodines were released into the atmosphere and resulted in exposure to millions of

people. The UA and BY populations suffered the heaviest exposures. Thousands of workers (or "liquidators") were also exposed to very high levels of radiation while fighting fires, stabilizing the site, and cleaning up the area. Many workers were placed at risk for the development of leukemia and other diseases.

The human, environmental, and political consequences of this disaster were enormous. An estimated 30 to 40 workers died in the immediate aftermath of the disaster, some because of accidents, but more deaths were because of acute radiation exposures. Health care systems were overwhelmed, and thousands of people were evacuated from heavily contaminated areas, many never to return to their homes.

The Union of Soviet Socialist Republics (USSR) initially resisted offers of assistance from the U.S. In 1987 however, Presidents Ronald Reagan and Mikhail Gorbachev met and discussed the need to cooperate in civilian nuclear reactor (CNR) safety. This discussion led to the 1988 "Memorandum of Cooperation (MOC) in the Field of Civilian Nuclear Reactor Safety between the United States of America and the Union of Soviet Socialist Republics." The agreement was signed by the U.S. Nuclear Regulatory Commission (NRC) on behalf of the U.S. Government and the USSR State Committee for the Utilization of Atomic Energy. The MOC covers the following four areas of cooperation:

1. "Policy and practices of regulatory activity regarding safety of CNRs;

2. Problems of safety in design, construction, training, operation and management of CNRs;

3. Research directed at improving the safety of CNRs; and

4. Questions on health effects and environmental protection requirements arising from the use of CNRs."

The MOC did not specify that human health studies be conducted as a result of the Chernobyl explosion, but the document established the framework for eventual NCI involvement in Chernobyl health effects research in UA and BY.

History of NCI's Involvement in the Chernobyl Health Effects Studies

The MOC specified that a "Joint Coordinating Committee for Civilian Nuclear Reactor Safety" (JCCCNRS) be established to coordinate and ensure the implementation of the

agreement. The JCCCNRS was equally represented by U.S. and USSR members. The MOC allowed the JCCCNRS to establish working groups for "exchanges of scientific and technical safety information" related to CNRs. Under the MOC, Working Group 7 (WG7) was established to address health and scientific issues, including research on Chernobyl-related health effects; DOE served as the lead for the U.S. In June 1990, U.S. WG7 members and USSR counterparts met in Kiev to begin discussions on several Chernobyl health effects issues, including the need to conduct Chernobyl-related dosimetry and epidemiologic studies related to thyroid disease among children and leukemia among liquidators. Drs. Robert Miller and Gilbert Beebe[4] were asked to participate as task leaders to continue further discussions and develop plans to conduct the studies.

Immediately after the explosion, scientists throughout the world began to consider the potential health toll and scientific issues related to the accident's aftermath. Scientific understanding of the risk of thyroid cancer and thyroid disease among children is hampered by the lack of data on internal doses of I-131. The large population exposed to radioiodine and expectations that varying radiation doses (exposure levels) of the population could be calculated presented a unique scientific opportunity. An assessment could be made of the extent to which exposure to radioiodine, especially I-131, in varying exposure levels (doses), leads to thyroid cancer and other related thyroid diseases over time. Since children are more at risk for radiation-induced thyroid cancer than adults, the population for the UA and BY thyroid studies was defined as children exposed at the time of the accident.

Similarly, information on the effects of I-131 exposure and leukemia are very limited and such studies can help elucidate the relationship between leukemia and exposures to ionizing radiation. (The relationship between leukemia and exposures to ionizing radiation was primarily known from studies of Japanese atomic bomb survivors; however, data from these studies were limited because few young adult Japanese males were exposed because they were elsewhere in military service and only minimal information had been collected on the effect of low and moderate radiation exposures and the development of leukemia.)

The potential public health relevance of the proposed thyroid disease and leukemia studies was (and continues to be) that findings could be used by UA and BY health authorities to plan for the disease burdens in their populations that might be caused by

[4]Drs. Miller and Beebe were NCI employees, but their participation was as experts rather than official NCI representatives. NCI's official involvement in the studies did not begin until the NCI/DOE Interagency Agreement was executed on September 19, 1990.

these exposures, and to assist public health planning and response in the event of future, similar disasters elsewhere in the world.

In December 1990, U.S. and USSR scientists met in Chernigov and Kiev. These meetings put into focus the divergent positions between the two groups. While the primary interest of U.S. scientists was assessing possible thyroid disease and leukemia caused by varying doses of radiation exposure from the Chernobyl reactor explosion, the USSR's primary interest was in securing U.S. technical assistance, medical equipment, computers, and other resources to support its medical and public health efforts related to diagnostic screening, clinical examinations, and treatment of affected populations. The USSR was less interested in long-term and highly structured epidemiologic investigations. During other site visits to the USSR by NCI and its collaborators to explore prospects for conducting the studies, additional challenges were identified that would hamper NCI's progress:

- overestimation by USSR scientists about finances and other resources available from the U.S.;
- non-availability of the world's scientific literature to USSR scientists;
- lack of experience among USSR scientists in a research culture of collegial collaboration, mutual cooperation, and coordination to more effectively resolve problems;
- inconsistent levels of training and expertise in scientific research and methods, particularly chronic disease epidemiology;
- inadequate laboratory and clinical facilities;
- outdated medical and computer equipment;
- resistance by USSR scientists in allowing U.S. scientists to access their Chernobyl-related data; and
- location and recruitment of large study populations and long-term retention of them in the studies.

The breakup of USSR in 1991 led to political and economic instability in the newly independent states of UA and BY, which added to NCI's challenges. Moreover, lead

project managers and key scientific staff in the Health Ministries of both countries frequently changed during the next several years. In an attempt to strengthen the collaboration with UA and BY health authorities, NCI made two critical decisions. First, NCI and USSR scientific leaders acknowledged that the health needs of Chernobyl-affected citizens were of primary importance, but credible research could be successfully and simultaneously conducted. Second, the studies would be the domain of UA and BY, but NCI and its partners would provide technical assistance, equipment, and other necessary resources to conduct the studies. On the one hand these agreements allowed the studies to progress; on the other hand, the research studies were still of lesser importance to UA and BY compared to the provision of health care. While NCI's position limited its ability to argue for changes and improvements in the studies, including having full access to data, there was legitimate concern on NCI's part that these studies would not be able to be implemented unless it compromised on these points.

As the lead member of WG7, DOE involved NCI and other scientific personnel in plans to conduct the thyroid and leukemia studies. By August 15, 1990, DOE approved NCI's request for funds to support "U.S.-Soviet Joint Research on the Biomedical Effects of the Chernobyl Reactor Accident." In a September 17, 1990, letter to NCI, DOE's Associate Director for Health and Environmental Research noted that thyroid disease and leukemia were to be the primary research issues of interest. The Associate Director also stated that "it remains to be determined whether efforts to collaborate with Soviet scientists in studies of health effects will have scientific promise and merit long-term funding" and "DOE is hoping that a decision can be made by December 31, 1991, whether to proceed with specific studies." The Associate Director recommended that NCI select Dr. Bruce Wachholz (an NCI employee) to manage an Interagency Agreement (IAG). On September 19, 1990, the IAG was executed between DOE and NCI; DOE transferred $100,000 to NCI to implement the feasibility activities.

On December 19, 1991, a second IAG was executed to include the period through September 30, 1992. DOE would transfer an additional $112,500 for NCI's FY 1992 operations. NCI's responsibilities were outlined in the "Description of Services."

> "This agreement is a mechanism to implement the transfer of funds for Chernobyl-related studies in FY 1992 from DOE to HHS, NCI. NCI will assume responsibility for coordination with Soviet counterparts in the design, implementation, analysis, and scientific interpretation of leukemia and thyroid disease epidemiology studies of Chernobyl exposed populations in the Soviet Union. The activities will be directly managed by NCI."

The IAG also directed HHS (in practice, NCI) to provide "Periodic Financial and Technical Reports to DOE as agreed upon." The IAG marked the beginning of NCI's official involvement in the Chernobyl studies and was signed by NCI's Assistant Director and DOE's Deputy Assistant Secretary in the Office of Health. The IAG's specified Project Officers were Dr. Bruce Wachholz of NCI and Dr. Harry Pettengill of DOE. NCI initially assigned three full-time persons on the project: Dr. Wachholz, Chief of the Radiation Effects Branch in the Division of Cancer Biology, and staff members, Drs. Gilbert Beebe and Andre Bouville. Additionally, in 1991, NCI hired a Ukrainian scientist, Dr. Olga Tsvetkova, to serve on-site in Ukraine in a scientific and management liaison capacity; she continues to this day to provide expert assistance to UA, NCI, and Columbia University scientists. Dr. Ihor Masnyk joined the NCI project staff in 1995. (Attachment V, Key Events)

This IAG did not specify goals, outputs, time lines, monitoring and evaluation processes, and reporting mechanisms. Over time, this lack of specificity led to misunderstandings and confusion between NCI and DOE about roles and responsibilities, as time passed and new senior staff, particularly at DOE, replaced the people who originally executed these early agreements. In March 1992, DOE sent an IAG to NCI with a "Standard General Provisions for DOE Interagency Agreements" attachment. The document was common to all agencies receiving funds from DOE and indicated that NCI would be required to submit progress and financial reports, and obtain prior written approval for international travel and meeting attendance. There were additional accountability requirements related to purchasing, owning, and maintaining equipment under a DOE agreement. NCI did not agree to the requirements for meeting attendance and particularly equipment purchases "due to questions of title, accountability, maintenance, safeguarding, and control." That is, since some if not all of the equipment that might be purchased would be destined for use by scientists in USSR, NCI was concerned about being held accountable for it. (An important related factor in this decision was that the National Institutes of Health (NIH) had just been audited for alleged property mismanagement and NCI was reluctant to assume this sort of responsibility in the audit environment extant at that time.) NCI's position was that DOE should purchase and be responsible for equipment. DOE subsequently contracted with Lawrence Livermore National Laboratory (LLNL) for all equipment and supply purchases after LLNL stepped forward and agreed to carry out this complex and critical function.

In 1994, NRC and DOE executed the "Epidemiologic Studies of Radiation Induced Thyroid Disease in Belarus and Ukraine" IAG. The purpose of the agreement was to "assist DOE in funding the epidemiologic studies of radiation induced thyroid disease in BY and UA conducted under the auspices of the Joint Coordinating Committee for

Civilian Nuclear Reactor Safety (JCCCNRS) Working Group7 (WG7) or similar letter arrangements for continuing cooperation." Under the IAG, NRC transferred $500,000 to DOE in FY 1994 for activities to be completed under the BY protocol. NRC also committed $500,000 of FY 1995 funds after the UA protocol was signed. No performance requirements were described in this IAG other than the requirement that DOE submit quarterly reports summarizing the expenditure of funds. No earlier NRC agreement that officially engaged DOE in the conduct of the studies has been identified.

NCI's Work

NCI faced formidable management and scientific challenges in its efforts to initiate and conduct the thyroid and leukemia studies. While many of the problems were beyond its direct control, NCI study staff often did not take appropriate steps to resolve or minimize major problems that developed prior to 1997. For example, there is no written evidence that assistance was sought from senior NCI managers to resolve scientific or management problems that arose with DOE, UA, BY, and other collaborators. Compounding these difficulties was an apparent lack of recognition on NCI's part that only three full-time NCI scientists were expected to implement a project with such an extraordinarily complex scientific mission.

As noted earlier, NCI declined to accept responsibility for purchasing supplies and equipment for the UA and BY studies when the initial DOE/NCI agreements were executed in 1991 and 1992; this responsibility was assumed by LLNL. (Dr. Lynn Anspaugh, a leading dosimetrist from LLNL who had played a key role in planning for and carrying out the studies, had engaged LLNL to assume responsibility for this because no other agency or organization was able to or stepped forward to accept responsibility for this complex function. LLNL's Ms. Sheilah Hendrickson led this procurement effort.) Dealing with the logistics aspects of the studies was a major undertaking with numerous complications. Initially, UA and BY scientists submitted lofty supply and equipment requests that at least in part reflected their continuing priority to obtain resources needed for the delivery of non-study related health care services to Chernobyl-affected populations. Additionally, the new governments of UA and BY established complex customs and taxation regulations that applied to supplies and equipment coming into the countries from all external sources, resulting in equipment embargoes and the possibility of major cost add-ons. Complications subsequently surfaced between NCI and LLNL as well as UA and BY scientific staff regarding everything from the timeliness to the composition of orders. For example, in some cases, some perishable supplies that had been delivered to UA and BY became outdated because UA and BY were not ready to implement certain aspects of the studies. The lack of study time lines made it very

difficult for LLNL to time shipments to match study implementation phases. Despite these obstacles, equipment and supplies needed to launch these studies were in place in 1995. In 1996, LLNL discontinued its role as NCI collaborator for procurement. (Later in 1996, NCI negotiated an agreement with the Veterans Affairs National Acquisition Center (VANAC) to become its procurement agent, but this proved to be an unsatisfactory long-term solution.) It was not until April 1999, when NCI's contract with Columbia University was expanded to include providing logistics support to the studies, that this procurement function was re-established.

Change in NCI/DOE Relationship Leads to Progress

Mounting frustration between DOE and NCI regarding the slow pace of the studies served as a catalyst for progress in three key areas. First, DOE and NCI senior management developed a productive and positive involvement in the studies. Second, recognition was made that significant resources and new study management approaches were needed to ensure the success of the studies. Third, a new IAG was developed that clearly defined responsibilities for both NCI and DOE.

New DOE staff became involved in the management of the DOE/NCI IAG and became far less inclined to give NCI the wide scientific and administrative latitude that it had enjoyed. Particularly beginning in early 1996, there began a series of charges and rebuttals between DOE and NCI related to DOE's perception of lax management of the studies by NCI, including NCI's failure to provide necessary progress and financial reports to DOE, and NCI in turn bridling against what it perceived to be micro-management on the part of DOE. Relatedly, NCI complained that it was being treated by DOE as if it were a contractor as opposed to a collaborating Federal agency. By February 1996, DOE staff independently (that is, without NCI staff accompanying them) conducted fact-finding site visits to UA and BY, which included assessing study-related issues with UA and BY study leadership. Additionally, DOE began to press NCI to establish an external scientific advisory body as had been specified in the thyroid and leukemia protocols; to begin providing DOE with project information, including progress and financial reports and information about which NCI staff were assigned to work on the studies; and to develop and implement study work plans. (DOE was at this time directly providing supplemental salary support to UA and BY scientists and began requiring work plans and UA and BY staff allocation information as a condition for continuing to receive this support. These documents began to be generated, however, the work plans tended to be little more than short-term, time-framed, and brief activity descriptions.)

On March 5, 1996, a DOE-sponsored "DOE/NCI/NRC Meeting to Discuss the Belarus/American Thyroid Study" was held that was attended by 15 individuals at varying organizational levels from the three agencies noted above and that also included representatives from the DOS, LLNL, and an NCI study collaborator from Cornell University. Among the NCI attendees was the Director of the Division of Cancer Biology (DCB), the Division that included the Branch that managed the Chernobyl studies, and DOE's Director, Office of International Health Programs. At this point it is clear that issues were becoming critical enough that they drew in more senior NCI and DOE staff as well as a DOS official. Even though the BY study was ostensibly the focus of the meeting, a review of the minutes of this meeting indicates that it focused almost exclusively on the organizational and relationship difficulties on the U.S. side that had begun to swamp the studies in both UA and BY. Problems were openly and frankly discussed and action items and agreements were developed designed to begin resolving problems. These included developing a set of responsibilities for each of the organizations involved in the studies, an agreement that NCI would begin to provide progress reports to DOE, and that NCI (as well as DOE and NRC) would provide information on overlapping studies conducted by other organizations in UA and BY to begin to determine ways to potentially develop collaborative efforts. It is notable that "The group agreed that . . . Dr. Anspaugh and his team at Livermore were doing an excellent job purchasing and shipping equipment and supplies to Belarus." The meeting closed with DOE indicating it would host another such meeting in May or June 1996 to continue discussions.

Despite apparent progress at this meeting, the relationship between the principal parties continued to be contentious. Also, these problems as well as the lack of progress with the studies "went public." On April 24, 1996, an Associated Press release reported on a group of Connecticut doctors (including one who was previously an NCI Chernobyl study collaborator) that criticized the U.S. Government for delays in the UA and BY studies. DOE is attributed in this release as identifying the delays to Eastern European political upheaval and to management problems with NCI. By May 1996, internal discussions were being held among NCI study and leadership staff about the wisdom of continuing NCI involvement in the studies, not on the basis of the potential scientific value of the studies or the challenges in carrying them out, but because of continuing external criticism and perceived external interference in NCI's conduct of the studies.

On July 15, 1996, a defining NCI/DOE meeting was held that included the Directors of NCI's Division of Cancer Epidemiology and Genetics (DCEG), DCB, and DOE's Deputy Assistant Secretary for Health Studies. The June 23, 1996, report of this meeting by the two NCI Division Directors to the Director, NCI, noted that:

- "the NCI study should not be subject to scientific or administrative oversight by DOE or its scientific review group";

- DOE expected to continue to provide partial financial support to NCI for the conduct of the studies;

- NCI could not continue to support the implementation phase of the studies with its limited internal staff and needed to issue a contract to increase scientific and logistics capacity; and

- a new IAG was necessary to define DOE and NCI roles and responsibilities.

In December 1996, the new IAG for FY 1997 was executed and signed by the NCI Director and the DOE Assistant Secretary for Environment, Safety and Health. (Attachment VI, FY 1997 NCI/DOE IAG). The new agreement stated that DOE would transfer up to $800,000 to NCI in FY 1997 for the conduct of the studies. Additionally, NCI would assume responsibility for all management and scientific aspects of the studies with staff and necessary contractors; assume responsibility for all official and scientific matters with UA and BY; serve as the sole point of contact for official project-related communications between U.S. agencies, UA and BY Health Ministries, and other collaborators; develop quarterly milestones for progress evaluation; authorize payment for UA and BY support; share all project reports with DOE and other relevant U.S. agencies; submit annual progress and financial reports to DOE; invite DOE observers to all NCI-sponsored "review and reporting" meetings; and contribute funds to the project that at least match DOE's investment.

It is noteworthy that this IAG ratified almost all of the responsibilities that NCI assumed or acted as though it had from the date of the second DOE/NCI IAG signed by both agencies five years earlier, on December 19, 1991. The failure to delineate the respective roles and responsibilities of DOE and NCI at the very beginning of their relationship and in the 1991 IAG was a major factor that led to misunderstandings, study delays, and damaged relationships that affected this program until 1997.

Along with these events, NCI also was preparing for the September 1998 Senate Hearing on its management of the radiation studies. Both Congress and the public were paying more attention to NCI's U.S. nuclear weapons fallout report which, although essentially completed in 1994, had not been released by NCI until 1997. It is notable that the same few NCI staff that were working on the Chernobyl studies were also the same staff that

worked on the fallout studies. While the Hearing did not specifically focus on or determine whether either or both studies were in part delayed because too few NCI staff were involved in these two complex research endeavors, it would appear to be a logical assumption.

Despite these management complications, the NCI study team and its collaborators were also attempting to make progress on the thyroid disease and leukemia studies in UA and BY. From the outset of its involvement in the thyroid studies, NCI was assisted by an ad hoc group of both Government and non-Government radiation scientists. This group, the **F**allout **R**adiation **E**ffects on the **T**hyroid group, or "FRETTERS," included NCI scientists Drs. Wachholz, Beebe, and Bouville, as well as Dr. Anspaugh from LLNL, in its core membership of ten. FRETTERS participated with NCI, UA, BY, and other scientists in thyroid study protocol development, served as technical advisors to NCI, and frequently accompanied NCI staff on site visits to UA and BY. The group disbanded in 1996. (Attachment VII, FRETTERS members and affiliations). Another ad hoc group of scientists provided advice and assistance to NCI on leukemia study issues, including protocol development and review.

In addition to the challenges of implementing scientific projects in these two countries described earlier in this report, NCI faced additional and equally daunting ones as they began to work in earnest with the UA and BY scientific staffs.

It needs to be noted that slow progress in getting these studies operational was not due to lack of commitment, effort, or scientific skill on the part of the NCI staff and its collaborators. These scientists were recognized experts in various facets of radiation health effects research. Numerous, lengthy site visit trips were made to the two counties that accounted for thousands of person hours. Unfortunately, progress came very slowly. In addition to those described earlier in this report, numerous other factors contributed to lack of progress, including the following:

- NCI's decision to serve as consultants/providers of technical assistance to its UA and BY colleagues by definition limited its ability to aggressively press for needed improvements and progress. Site visits often included large numbers of people on the NCI, UA, and BY teams and meetings (as reflected in the trip reports reviewed by SMRCS) were often "plenary," large-group discussions that often focused around reports to NCI by UA and BY staff with advice and guidance offered by the NCI team. Site visits appeared to lack continuity from one visit to the next; problems and accompanying recommendations dealt with on one site visit did not

appear to be followed-up to assess progress on implementing recommendations on subsequent site visits.

- NCI did not appear to take full advantage of potential collaborative opportunities that existed in UA and BY. There were researchers from several different countries (e.g., France, Germany, and Japan) working on similar research issues. Although NCI staff and collaborators attended international meetings and conferences that focused on all Chernobyl research being conducted, and presented scientific papers at these forums, the primary emphasis among the various study sponsors seemed to focus more on avoiding overlap than on effecting collaboration. This was unfortunate given the limited staff and financial resources of the U.S. study sponsors, study complexity (both scientific and logistic), and the political complexities associated with conducting studies in UA and BY. An exception to this was NCI's dosimetrist, Dr. Bouville, who had established productive international collaboration among dosimetrists. (SMRCS strongly supports NCI's current plan to convene a meeting of all Chernobyl researchers to share information and identify collaborative opportunities.)

- Because of NCI's inability to coordinate and utilize supplies and equipment–at least in a manner that met UA and BY expectations-- it lacked influence to generate improvements in UA and BY operations. UA and BY were participating in these studies in part because of the prospect of receiving this type of support, and without it their cooperation and commitment to carrying out the studies was less than enthusiastic. Another tactical error was the early decision to expect the UA and BY Governments to provide supplemental salary support to their scientists. In fact, both Governments lacked major financial commitments to the studies and both (particularly BY) did not have the financial resources to supplement scientists' salaries. In 1996, DOE began providing supplemental salary support for UA and BY study staff.

- Leadership and staff instability in UA and BY made it difficult to know from one site visit to the next who was to be in charge of or involved in the studies. While such problems were resolved relatively quickly in UA, they persisted in BY at least through 1995.

Despite these problems, NCI was able to ensure the development of thyroid disease and leukemia research protocols with UA and BY. The protocol for the study of thyroid cancer and other thyroid disease was executed with BY in 1994; and with UA for the study of thyroid cancer and other thyroid disease in 1995, and for the study of leukemia

and other hematologic diseases among clean-up workers in 1996. Additionally, Institutional Review Boards (IRBs) were established in UA and BY, and the thyroid disease and leukemia protocols were approved by the NCI IRB and the NIH Office for Protection from Research Risks. The execution of these protocols was accompanied by "Arrangements for Cooperation," essentially agreements between the U.S. and the Health Ministries of UA and BY. The two thyroid agreements' sole signatory on the U.S. side was from DOE. The terms of these agreements were virtually the same, specifically that the Ministries of Health of each country would provide the staff, their salaries, and facilities for the studies, and DOE would provide supplies, equipment, technical assistance, and professional staff training. The signatories of the "Arrangement for Cooperation" for the leukemia study were staff representing NCI, DOE, NRC, the UA Ministry of Health, and the UA Academy of Medical Sciences. The terms of this agreement were similar to the thyroid agreements, with the major exception that it notes that NCI, in conjunction with DOE and NRC, would provide "supplemental salary support" for UA scientists. (This was not a unique feature of the leukemia protocol–by 1996 there was recognition on the U.S. side that this salary support was necessary to ensure scientific staff stability and to compensate the UA and BY scientists for their additional work loads.)

Executing the protocols did not signal accelerated progress on implementing the protocols. That was not to occur until beginning in 1997.

On March 7, 1997, NCI issued an open-competition Request for (contract) Proposals (RFP) titled, "Technical and Scientific Support and Management for the Project, Effects of the Chernobyl Accident on the Incidence of Thyroid Cancer and Luekemia/Lymphoma in Belarus and/or Ukraine." The issuance of this RFP followed through on NCI's recognition, as reflected in its December 1996 IAG with DOE, that it did not have sufficient staff to manage the implementation of these studies. Columbia University successfully competed for this contract for epidemiologic studies of thyroid disease, leukemia, and lymphoma; the contract was awarded to Columbia University in September 1997.

The contract's Principal Investigator at Columbia University was and remains Dr. Geoffrey Howe, an internationally respected radiation epidemiologist. Dr. Howe has had significant international experience, including work in the aftermath of the Chernobyl accident on various efforts related to the study of leukemia among Ukrainian liquidators. Dr. Howe rapidly assembled a stellar team of senior, experienced scientists and managers (most of whom are on staff at Columbia University) to join him on his team in such specialty areas as quality assurance/quality control (QA/QC), endocrinology, laboratory

sciences, epidemiology, logistics and finance, cytology/pathology, biostatistics, data management, hematology, radiation biology, and radiation dosimetry. Additionally, Columbia University has hired two people (one from Russia and the other from UA) who understand the setting the study team is working within in UA and BY, and who can help ensure the accurate translation of materials).

Dr. Howe and his group are effectively carrying out their contract responsibilities. By December 1997, just three months after NCI issued the contract to Columbia University, team members had visited UA to review leukemia study progress, held briefing meetings with NCI staff, and developed a work plan for the second quarter. By the end of the second quarter of operations, Dr. Howe's team had conducted comprehensive assessments of the status of operations in UA and BY. The team identified numerous operational problems that included: remaining training needs among some key UA and BY staff, locating and recruiting study participants, lack of effective data management and associated backlogs in data entry, overly complex and unlinked records systems, and QA/QC concerns that spanned most of the study components. The Columbia University team immediately began to address these problems.

Columbia University's management approach to these studies is efficient and directive. When site visits are conducted (and there are frequent team visits to UA and BY, almost all including Dr. Howe as well as NCI staff), team members meet one-on-one with their speciality area counterparts. When problems or deficiencies are identified, often immediate hands-on assistance is provided to solve the problems. For more complicated problems, solutions are discussed and agreed on with UA and BY staff and the team follows through on subsequent site visits to make sure steps are being taken to resolve the problems. Significant efforts are being made to streamline and improve the efficiency of the logistical aspects of the studies. For example, in UA, Dr. Howe's group found that numerous different forms had been created for each study subject; efforts are now being led by an NCI scientist to reduce this paperwork volume. Additional efforts are being made to standardize records and data items so that they are the same for both countries. (Currently, common dosimetry forms are being used in both countries.) Substantial progress to re-establish logistics operations has been made by Columbia's project manager/logistics specialist. Goals, and plans to achieve these goals have been developed and implemented.

The important dosimetry efforts in both UA and BY have remained consistent and on track even during early management disruptions. This is apparently because of the expertise of NCI scientist Dr. Andre Bouville (as well as his long-time dosimetry collaborators) who

has long been accepted as a collaborator and leader by the dosimetry teams in both countries.

The dosimetry data, derived largely from one-time measurements of radioactivity in the thyroid, differs in quality between UA and BY. Most of the measurements on Ukrainian people were made by collimated and calibrated instruments. The measurements of the Belarusian people are of lower quality, but this is recognized and correction factors derived from the Ukrainian measurements are being applied to the data.

Common dosimetry forms have been developed for use in both countries. Information such as diet, location, and the use of prophylactic potassium iodide will be used along with the one-time thyroid measurements to estimate the amount of exposure to I-131 over time and to calculate the thyroid doses. Where possible, other environmental dose reconstruction techniques are being used to validate the thyroid dose estimates and to provide information on uncertainties.

The scientific feasibility of these studies has remaining problems and challenges which require new protocols and continuous review by a group of independent peer scientists and citizen and public interest group representatives. The basic design which selects a sample of the original population and then conducts screening of the population to detect thyroid cancer and possibly other diseases is appropriate. However, the population was initially identified primarily through addresses on medical records which means those who were symptomatic or concerned about disease because of a high dose were probably seen first. These subjects as well as those who were seen in other studies or even in the course of normal medical care can create problems of interpretation in analyses because of treatment, a factor which has not been discussed in the protocols. Methodologies for uncertainty and sensitivity analyses need to be included in all phases of these studies.

Treatments which they have received from other sources, especially surgery as a result of screening, may interfere with the course of development of thyroid cancer or disease creating a challenge in utilizing these cases in calculating incidence of outcomes. The protocols have not discussed this problem.

There are continuing challenges which must be met in terms of trying to follow this population. The initial identification has been through medical sources meaning that many in the population have been seen because of illness or high estimated radiation doses. Unless the total sample can be found, this selection of the initial respondents who have been studied before protocols were initiated will tend to bias any results.

The exposed population of children is now 14 to 30 years of age. Thus, the "population" must include not only the study subjects that need examination, but, in most cases, parents of the subjects from whom the study teams must obtain information on food consumption around the time of the accident for dosimetry calculations. This means that for many potential study subjects, two addresses must be obtained, the address of the subject himself/herself, as well as their parents. Motivating subjects to participate in the studies after locating them has proven to be difficult; however, the Columbia University team and NCI staff as well as the UA and BY study teams recognize this problem and have been directing efforts to improve participation levels. As examples, creative health education and motivational materials have been developed in UA that have, coupled with modest cash incentives to defray the subjects' costs of attending clinics, markedly improved participation levels. Efforts to transfer these techniques to BY are under way. Although local political and citizen involvement in such national studies is a concept little understood in UA and BY, staff in both countries are beginning to utilize the expertise of local leaders to help publicize and support the studies, particularly in efforts to locate study subjects. This dynamic, if patiently and skillfully supported by NCI and Columbia University staff, could lead to expanded public participation in these studies. Additionally, both UA and BY employ mobile teams that are becoming increasingly successful in bringing screening to people in rural areas and this too, has improved subject participation levels. An additional issue is that subjects might have been seen as part of other studies or just in the course of normal medical care. If they received treatment, it may be difficult to obtain the information on these subjects and to determine that the diagnostic criteria for therapy were similar to those of cases seen under the current protocol.

As soon as these issues are addressed, the operations need to be periodically re-evaluated to determine the success of the efforts. The studies are predicated on repeat visits by the subjects for possibly up to 20 years. The success of the teams in assuring the subjects' continuing cooperation into the future needs to be assessed quarterly in order to determine how long the study follow up may be feasible.

The thyroid studies have other important issues that need to be addressed. The studies are being conducted by UA and BY scientists and they retain the data generated by the studies (although Columbia University and NCI scientists have full access to the data while in UA and BY). Formal agreements need to be established that allow data to be fully available to NCI and Columbia University scientists, and after this is accomplished, ultimately to have these data be available to other researchers for independent analyses. If not, alternative methods of ensuring the quality of the information and access to the data for analysis must be developed. NCI and Columbia University staffs recognize this as a priority issue to be addressed. Access to data from other investigators or from previous diagnoses and

treatments must be assured. NCI is encouraged to follow through on its plan to have a meeting of these other investigators so that these issues can be discussed and resolved. SMRCS recommends that such meetings be widely advertized and open to interested scientists and the public. Additionally, SMRCS recommends that a meeting proceedings report be developed and disseminated. This report should catalog and summarize all Chernobyl research efforts supported by other countries, agencies, and organizations.

The exact length of the thyroid studies has not been determined, although they are expected to continue for at least ten more years, and possibly up to 20 years. Long-term continuity and stable funding availability and commitments over time are concerns with all such lengthy, Federally-funded projects. The biostatistical issues surrounding longitudinal studies with screening where the medical decisions, such as removal of benign nodules, could influence study results and needs to be addressed. The procedures and timing for publication of study results (including interim analyses and findings where appropriate) in conjunction with UA and BY scientists and the methods of communicating these results, that is, a publication plan, have not been addressed but needs to be developed promptly. Full access to data and a publication plan are essential to ensure that affected populations do not receive different answers to their health concerns from different research groups using different analytic methods and data sets. Unless all of these issues are clarified soon, delays and internal problems can arise as the studies are being completed.

Additionally, the study still needs to further review the goals and methodologies under which the projects are being conducted. The feasibility of the project, adherence to goals, and appropriate management needs to be assessed by a peer review group independent of NCI or the contractor. This was suggested by the Bi-National Review Group in a recent report. That peer review group should be large enough to include all scientific disciplines involved in the studies and should be comprised of individuals who have not had involvement in these NCI studies from their inception. It should include liaison members from the Bi-National Review Group even though its members may have had long-term involvement in the studies. This group should provide advice and recommendations to NCI regarding appropriate funding levels for the studies. This group should also review interpretation of study results. This peer review group should also include a public input component, a step that was not included in the Bi-National Review Group's recommendations.

Public input in the U.S.-based peer review group should include concerned citizens as well as representatives of relevant public interest groups. The value of public input and involvement in Government-sponsored studies recognizes citizens are integral to ensuring the successful execution of these studies through the provision of advice, assistance, and

oversight. It recognizes that the best science is done when conducted openly and helps ensure that the results of research are communicated in a timely manner and in terms that can be understood by all citizens.

Questions Developed by HHS to Assess NCI's Conduct of the Chernobyl Studies

The HHS questions and SMRCS responses are outlined below:

(1) What was the NCI asked to do with regard to the study of the impact of the 1986 Chernobyl nuclear reactor meltdown on the incidence of thyroid cancer and leukemia in BY and UA? (2) Who requested that NCI conduct this study? (3) What was the context for this request? (4) What study scope and output were requested? (4) What time frame was specified? **Response:** The focus of this Committee review was on the collaboration with BY and the UA, which involves thyroid cancer and thyroid disease. The leukemia study is an occupational study of post-accident workers and is still in a feasibility mode. (1) NCI staff became involved with DOE on Chernobyl study issues as colleagues and consultants prior to official NCI involvement. (2) On September 19, 1990, an IAG was executed between DOE and NCI that transferred $100,000 from DOE to NCI to carry out the feasibility efforts. (3) The agreement was a mechanism to implement the transfer of funds for Chernobyl-related studies in FY 1992 from DOE to NCI. NCI committed to assuming responsibility for coordination with Soviet counterparts in the design, implementation, analysis, and scientific interpretation of leukemia and thyroid disease epidemiology studies of Chernobyl exposed populations in the Soviet Union. (4) The IAG did not otherwise specify goals, outputs, time lines, or monitoring and reporting processes.

1. (1) What did NCI commit to in response to this request? (2) Who spoke for NCI and in what context in making this response? (3) What kind of study and what methodology did NCI propose? (4) What goals, timetables, milestones, and monitoring and reporting processes were agreed to? (5) What study outputs were agreed to? (6) What next steps were anticipated? **Response:** (1) The agreement was essentially a good-faith agreement between the two parties without any specifics as reflected in the IAG. (2) Dr. Elliott H. Stonehill, NCI's Assistant Director at that time, signed the IAG. (3) NCI proposed an occupational leukemia study and a thyroid disease epidemiology study, but methodologies were not specified in the initial agreement. (4)-(5) No goals, timetables, milestones, and monitoring and reporting processes were agreed to; reporting requirements were non-specific. (6) While broad latitude was provided to NCI under the agreement, the lack of specificity and the broad scope of the agreement led to confusion about roles and

responsibilities over time. (6) Outputs and time lines were not specified. As previously noted in this report, NCI agreed in its FY 1992 IAG with DOE to " . . . assume responsibility for coordination with Soviet counterparts in the design, implementation, analysis, and scientific interpretation of leukemia and thyroid disease epidemiology studies of Chernobyl exposed populations in the Soviet Union."

2. How did NCI carry out this project?

A. Who was in charge of this project? **Response:** Dr. Bruce Wachholz, NCI's Chief of the Radiation Effects Branch, DCB, and staff members, Drs. Gilbert Beebe and Andre Bouville, were the full-time NCI staff members on the project. Additionally, Dr. Olga Tsvetkova was employed by NCI in a science liaison capacity in UA. Dr. Ihor Masnyk joined the project staff in 1995. Dr. Wachholz was the designated Project Officer on the initial IAG with DOE.

B. (1) What NCI staff and other resources were committed to and actually used for the project? (2) What staff and resources from entities other than NCI were committed to and used for the project? **Response:** (1) As noted previously in this Report, three U.S.-based NCI scientists originally participated on the project; NCI currently has four scientists (and the additional scientist working on-site in UA) working on the project with numerous other allied NCI staff providing varying levels of additional scientific, management, and administrative support. The 1997 addition of Columbia University as an NCI contractor for scientific and logistics support has substantially expanded the staffing base of the project. NCI financial resources (including staff salaries) committed to the project for the period FY 1991-FY 1999 totaled $7,131,800, including $1,471,361 in FY 1999. (2) As previously noted in this report, numerous staff from DOE and LLNL, as well as colleagues from academia (e.g., some FRETTERS members) provided varying but substantial levels of services to this project over the years, much of it without compensation. DOE and NRC have provided the bulk of the additional financial support to NCI over the years. During the FY 1991-FY 1999 period, DOE has provided $2,322,000 and NRC has provided $834,300 (in FY 1997).

C. What is the timetable of key events that defined the course of the project? **Response:** See Attachment V.

D. To what extent did the actual course of the project fit projected goals, timetables and milestones? **Response:** No expectations were initially made; no goals, timetables or milestones to guide the studies and measure progress were developed until recently.

E. What problems were encountered (within the USSR)? **Response:** (1) An overestimation on the part of USSR scientists about finances and other resources available to them from the U.S.; (2) lack of availability of the world's scientific literature in the USSR; (3) lack of experience among USSR scientists in a research culture of collegial collaboration and mutual cooperation to more effectively coordinate work and resolve problems; (4) inconsistent levels of training, expertise, and experience in almost all aspects of scientific research and scientific methods, particularly chronic disease epidemiology; (5) inadequate laboratory and clinical facilities; (6) outdated medical and computer equipment; (7) resistance by USSR scientists in allowing U.S. scientists to have access to Chernobyl-related data; (8) difficulties in locating, then recruiting and retaining large study populations long-term; and (9) delays in progress due to political and economic instability caused by the breakup of USSR and the creation of the newly independent countries of UA and BY.

F. What steps were taken to deal with these problems? **Response:** Problems were often resolved haphazardly as they arose; no systematic approach apparently was developed. This led to ad hoc decision-making and inconsistent project management. These problems as well as the lack of study time lines hampered LLNL's ability to efficiently supply equipment and other materials to UA and BY scientists.

G. Was any outside assistance requested to deal with these problems? **Response:** No written evidence was found that significant assistance from external sources or NCI senior management was requested.

H. Were revised goals, timetables, and milestones developed? **Response:** General goals and work descriptions were embedded in the protocol, but no timetables were specified.

I. Were any lines of inquiry discontinued? **Response:** No direct activities were discontinued after acceptance by NCI as part of the research agenda.

3. (1) What other agencies or organizations collaborated with NCI in the conduct of the study? (2) How do each of the parties assess this collaboration? **Response:** (1) The major NCI collaborators were DOE, FRETTERS, LLNL, and the Ministries of Health of BY and UA. (2) Past records document a history of problems with collaboration between DOE and NCI, but current collaboration between the two agencies is satisfactory. Current collaboration between the U.S., UA, and BY appears to be satisfactory. Collaboration between UA and BY is just beginning. Collaboration among dosimetrists has been productive and long-standing among the three countries. LLNL is no longer collaborating on this project either for logistics or for dosimetry expertise.

4. How were study progress, problems, and remedial changes reported to the NCI Director, the NIH Director, the HHS Secretary, and Congress? **Response:** No written evidence indicates that a reporting mechanism was developed until 1996 when DOE senior leadership met with study principles to begin to address problems affecting the studies. Outside entities often brought problems to the attention of senior management levels.

5. (1) What is the current status of this project? (2) What are current goals, timetables, milestones, allocated staff and resources, study scope and methodologies? **Response:** (1) In 1999, NCI transferred the Chernobyl studies from DCB to the DCEG's Radiation Epidemiology Branch (REB). The transfer of the studies to NCI's Division of Cancer Epidemiology and Genetics has significantly enhanced scientific and management oversight of the studies. A Chernobyl Research Unit was established under Dr. Gilbert Beebe's leadership. Dr. Ihor Masnyk was named the Project Director and the point of contact with Columbia University. NCI has hired additional staff for this activity as well. DCEG Director Dr. Joseph Fraumeni, DCEG Deputy Director Dr. Shelia Zahm, and REB Chief Dr. Elaine Ron take an active approach to ensure the effective management of the studies. NCI's Director and Deputy Director are fully informed about study progress and are supportive of staff involved in these studies. The SMRCS site visit to the UA and BY projects found a highly motivated, effective, and increasingly well-trained staff. It should be noted that many committed scientists from NCI, DOE, LLNL, and academia worked on the studies for many years and under challenging circumstances. An important legacy of their work is a well-equipped and trained cadre of research and medical personnel in UA and BY. NCI, Columbia University, and others are continuing the process of strengthening this model. This alone will benefit UA and BY citizens long-term. UA and BY scientists and their U.S. counterparts at NCI and Columbia University appear to have developed effective working relationships. In November 1999, NCI hosted a landmark conference that for the first time brought NCI,

Columbia University, and UA and BY scientists together in one place to share information and develop new approaches to accelerate progress. Commendably, NCI plans to periodically host these joint meetings. The Appropriations Conference Report also recommended that a financial audit of the studies be undertaken. In September 1999, NIH undertook this effort that included reviewing funding that was provided by DOE and NRC to additionally support the studies. NIH's Office of Management Assessment concluded that NCI complied with all financial requirements with the exception of providing financial reports to DOE. According to the audit report, DOE and NCI resolved this problem. (SMRCS confirmed this statement with a DOE official.) The scientific and logistics capacity of the studies has also been strengthened with the 1997 addition of Columbia University as NCI's science and logistics contractor. NCI also maintains an in-house advisory group comprised of NCI and other NIH staff that regularly meets to review progress and establish objectives. It also maintains the U.S. component of a Bi-National Advisory Group comprised of four leading, non-governmental radiation scientists that generally is established to provide scientific oversight; however, the roles and functions of this Group need to be clarified. (2) The thyroid studies are fully operational in UA and BY. An immediate and overriding goal for the thyroid studies is to conduct medical screenings of approximately 10,000 to 12,000 study subjects in UA and the same number in BY by the end of calendar year 2000 (UA and BY have reported that they each have screened approximately 7,000 study subjects as of April 2000). (Note: Initially NCI calculated that cohorts of up to 65,000 people were required; however, Columbia University scientists have completed power recalculations and have determined that 10,000 to 12,000 cohort sizes for each country is sufficient.) Phase I (the feasibility phase) of the leukemia study in UA has recently been completed and a protocol for a more limited retrospective leukemia study is under final development. Goals and objectives for this study are also under development.

6. (1) What has been learned to date through this project? (2) To what audiences and through what media has information been communicated? (3) What criteria have been used to decide what information can be communicated to whom and when and how? **Response**: (1) To date, the project has produced dosimetry results which allowed the projection of the number of subjects needed for the health study. Models have been created and will be utilized in the questionnaire. (2) The research to date primarily has been presented to professional audiences. Dosimetry procedures and methodologies have been published in peer review literature. (3) As previously noted, communication and publication plans need to be developed by the parties currently involved in the studies.

7. (1) What are the expected outcomes of this study? (2) What are recommended next steps to follow up what has been learned through this study or what further lines of inquiry would be useful or necessary? **Response:** (1) The study is expected to obtain an estimate of health risks from exposure to varying levels of I-131. This information is essential to aid health authorities in predicting the impact of future exposures to I-131. (2) Follow-up actions should include a determination of the total level of all thyroid diseases; determination of when the risk of thyroid cancer disappears; determination of when other endocrine abnormalities occur secondary to thyroid disease; completion of the study on leukemia; and development of a plan to describe public health measures to be implemented in the event of a similar accident; to improve dosimetric techniques; and to reduce potential public health problems.

8. In retrospect, what would have been ways to better manage this project to assure maximally effective use of resources and the timely development of needed information? **Response:** Roles and responsibilities should have been immediately defined and documented; IAGs that clearly delineated roles and responsibilities of various agencies should have been established; clear-cut management plans and evaluation procedures that included goals, time lines and management accountability should have been established; an independent peer review group that included concerned citizens and public interest groups should have been created at the outset; a system in which both DOE and NCI informed top management of the progress and problems should have been developed; and all parties should have more thoroughly analyzed the resources necessary to successfully implement a project of this complexity and scientific and public health significance.

RECOMMENDATIONS

The potential scientific value of the NCI Chernobyl studies is significant and they should be continued under NCI's leadership. While substantial progress has been made by NCI with regard to strengthening the scientific and management aspects of these studies, several significant problems must be addressed and promptly resolved to ensure their successful outcome.

In summary, it is recommended that NCI:

- revise and peer review the scientific protocols for the thyroid studies to include study goals, specific and measurable objectives, and time lines;

- assure access to UA and BY data and promote collaboration with other entities conducting similar studies;

- develop procedures to ensure that all logistical problems and supply and equipment needs are identified on an on-going basis and quickly resolved;[5]

- develop a peer review group of independent scientists, concerned citizens, and representatives from public interest groups to oversee the project and interact with the Bi-National review group;

- establish procedures to ensure accountability for reaching goals and time-lines that involve all participants;

- address methodological issues that may produce study bias;

- expand health communication activities to the public in BY and UA; NCI or Columbia University should consider employing a health education specialist to enhance this critical study component;

- develop a publication and communication plan that includes clear lines of responsibility for the various aspects of the interpretation, publication, and communication of study findings;

- develop a plan for the eventual development of a document that provides guidance for public health planning and response for similar disasters that may occur elsewhere;

- continue to enhance collaboration between BY and UA scientists; and

- ensure methodologies for including uncertainty and sensitivity analyses are included in all phases of these studies.

Acknowledgments

[5]During its site visit to BY, SMRCS noted remaining problems: timely delivery of some supplies from the U.S. to BY; efficient transfer of funds for supplemental salary support to BY study staff; and lack of methods for BY to provide modest incentives to increase participation levels of study subjects. The NCI and Columbia University teams must ensure that the UA and BY field units have the necessary equipment to overcome harsh conditions and maximize effectiveness while identifying and screening subjects in remote, rural areas. For example, computers need updating and lap top computers would be useful for field staff.

SMRCS wishes to acknowledge its appreciation for the excellent cooperation and openness of NCI management and staff during the course of this review; to the willingness of numerous individuals currently or previously involved in the studies from, or while with, NCI, DOE, LLNL, UA, BY, and Columbia University, who were interviewed and provided frank and important information essential for this report; and to the UA and BY Ministries of Health for their continued support of these studies. Additionally SMRCS wishes to acknowledge the contributions of Ms. Priscilla A. Patin and Mr. Art Schletty for their administrative and research support to the Subcommittee.

Attachment I

ADVISORY COMMITTEE FOR ENERGY-RELATED EPIDEMIOLOGIC RESEARCH

CHAIR

John R. Bagby, Ph.D.
Private Consultant

EXECUTIVE SECRETARY

Mr. Michael J Sage, M.P.H.
Associate Director for Planning, Evaluation, and Legislation
National Center for Environmental Health
Centers for Disease Control and Prevention

MEMBERSHIP

Mr. Gene Branham
Vice President
Fernald Atomic Trades Council

Mr. William H. Burke
Chief, Walla Walla Tribe
Confederated Tribes - Umatilla Indian Reservation

Mr. Wilfrid L. Cameron
Director, Education & Training Department
The Center to Protect Workers' Rights

H. Jack Geiger, M.D.
Arthur C. Logan Professor
Department of Community Medicine
City University of New York Medical School

Mr. Curtis Graves
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Associate Professor of Public Health
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F. Owen Hoffman, Jr., Ph.D.
President and Director
SENES Oak Ridge Inc.

Geoffrey R. Howe, Ph.D.
Professor of Public Health
Division of Epidemiology
Joseph L. Mailman School of Public Health of Columbia University

Genevieve M. Matanoski, M.D., Dr.P.H.
Professor, Department of Epidemiology
School of Hygiene and Public Health
The Johns Hopkins University

David M. Ozonoff, M.D.
Professor of Public Health and
Chair, Department of Environmental Health
Boston University School of Public Health

Genevieve S. Roessler, Ph.D.
Radiation Consultant

Mr. Richard H. Schultz
Administrator, State Division of Health
Idaho Department of Health and Welfare

Seth Tuler, Ph.D.
Research Fellow
Center for Technology, Environment, and Development
George Perkins Marsh Institute
Clark University

Attachment II

ADVISORY COMMITTEE FOR ENERGY-RELATED EPIDEMIOLOGIC RESEARCH (ACERER) SUBCOMMITTEE FOR MANAGEMENT REVIEW OF THE CHERNOBYL STUDIES

CHAIR

MATANOSKI, Genevieve M., M.D., Dr.P.H.
Dr. Matanoski is Professor of Epidemiology and Program Director, Occupational and Environmental Epidemiology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland. She has over 70 articles published in the peer-reviewed scientific literature; her major research interests include occupational and environmental diseases, environmental exposures including radiation exposures, cancer etiology, and evaluation of cancer control programs.

DESIGNATED FEDERAL OFFICIAL

SAGE, Michael J., M.P.H.
Associate Director for Planning, Evaluation, and Legislation
National Center for Environmental Health
Centers for Disease Control and Prevention

MEMBERS

BAGBY, John R., Ph.D.
Dr. Bagby is former Deputy Director of the National Communicable Disease Center (renamed Centers for Disease Control and Prevention-CDC) and former Director of the Missouri Department of Health. He has held academic appointment as Professor, Colorado State University, and is currently a Consultant in private practice specializing in the areas of environmental epidemiology and public health. Dr. Bagby is the Chairperson, ACERER.

ROESSLER, Genevieve S., Ph.D.
Dr. Roessler is Professor Emeritus (Nuclear Engineering Sciences), University of Florida, and is a Radiation Consultant in private practice. She is Editor-in-Chief, Health Physics Society Newsletter, and her fields of interest include health physics and radiation protection, radiation biology and dosimetry, radiation risk evaluation, and communicating information on radiation to the public.

SCHULTZ, Richard H., M.S.
Mr. Schultz is the State Health Official for the Idaho Department of Health and Welfare. Mr Schultz is responsible for six Bureaus, including Environmental Health and Safety, Clinical and Preventive Services, and Vital Statistics and Health Policy. He has major leadership roles in radiation-related health policy and health assessment activities both in the State of Idaho and in a multi-State area in the Northeastern United States.

Attachment III

PERSONAL INTERVIEWS CONDUCTED BY SMRCS–LIST OF INTERVIEWEES

National Cancer Institute

1. Dr. Alan Rabson, Deputy Director, National Cancer Institute (NCI)
2. Dr. Shelia Zahm, Deputy Director, Division of Cancer Epidemiology and Genetics (DCEG), NCI
3. Dr. Elaine Ron, Chief, Radiation Epidemiology Branch (REB), DCEG
4. Dr. Gilbert Beebe, Chief, Chornobyl Research Unit (CRU), REB
5. Dr. Ihor Masnyk, Chornobyl Research Project Director, REB
6. Dr. Andre Bouville, Dosimetrist, REB
7. Dr. Bruce Wachholz, Chief, Radiation Effects Branch, Division of Cancer Biology, NCI

U.S. Department of Energy

1. Mr. Barrett N. Fountos, Office of International Health Programs, U.S. Department of Energy

Columbia University

1. Dr. Geoffrey R. Howe, Professor of Public Health, Columbia University

Lawrence Livermore National Laboratory

1. Ms. Sheilah M. Hendrickson

Ukraine

1. Professor Mykola D. Tronko, Project Director and Director, Research Institute of Endocrinology and Metabolism
2. Dr. Anna Derevianko, Epidemiologist
3. Dr. Tetiana Bogdonova, Chair, Pathology Laboratory and Chief of the Project Pathology Group
4. Dr. Olga Tsvetkova, On-site NCI Project Coordinator
5. Dr. Iryna Kairo, Leading Research Fellow and Deputy Chief of the Dosimetry Group

Belarus

1. Dr. Valentin A. Stezko, Project Director, Clinical Research Institute of Radiation Medicine and Endocrinology
2. Dr. Valery A. Rzheutsky, Lead Clinician

3. Dr. Victor Minenko, Lead Dosimetrist
4. Dr. Dr. Elena Buglova, Epidemiologist
5. Dr. Olga Polyanskaya, Quality Control/Quality Assurance Office, Head of Data Coordinating Center

Other

1. Dr. Lynn Anspaugh, Dosimetrist, formerly with Lawrence Livermore National Laboratory, currently with the University of Utah. Dr. Anspaugh was interviewed by SMRCS by telephone, June 22, 2000

SUBCOMMITTEE FOR MANAGEMENT REVIEW OF THE CHERNOBYL STUDIES
KEY BACKGROUND EVENTS AND TIME-LINE ITEMS AND STATUS

April 20-21, 1999

The Deputy Assistant Secretary, Office of Science Policy, attended meeting of the Advisory Committee for Energy-Related Epidemiologic Research (ACERER) and requested that ACERER carry out a Congressional request for a scientific and management review of the merits of the science and management of the National Cancer Institute's Chernobyl studies. ACERER agrees to consider this request.

MAY 27, 1999

ACERER members and others participated in a conference call to, among other agenda items, discuss and act upon the HHS request to conduct the Chernobyl review. The quorum of ACERER members on the conference call voted unanimously in favor of conducting the review. ACERER member, Dr. Genevieve Matanoski, agreed to serve as Chairperson of the ACERER Subcommittee formed to carry out this review. This Subcommittee was named, "Subcommittee for Management Review of the Chernobyl Studies (SMRCS)."

Hold SMRCS meeting in July 1999

–Purpose: Answer questions and plan a strategy pertaining to the ACERER review, including outlining the main tasks, assigning work, and identifying questions to be addressed in the review.

–Status: Meeting was held on July 20, 1999, and the issues were addressed.

Hold SMRCS Meeting in August 1999

–Purpose: Agree on scope of the review, review and discuss questions to be addressed in the review, and determine documentation and other information needed to complete the review.

–Status: Accomplished. The Subcommittee for Management Review of the Chernobyl studies (SMRCS) met on August 12. Affirmed that the broad scope of the review would include identifying the challenges and opportunities faced by Ukrainian, Belarusian, and National Cancer Institute (NCI) scientists in carrying out the thyroid and leukemia studies in Ukraine (UA) and Belarus (BY); determining the type and amount of input and involvement from local leaders and the public in these studies; and characterizing the nature and extent of the collaboration among UA, BY, and NCI scientists and NCI's US collaborators. Reviewed and adopted the document, "Draft Basic Questions for a Scientific and Management Review of the Thyroid and Leukemia Studies Being Conducted by the United States and the Governments of Belarus and Ukraine (attached)," provided to SMRCS by Dr. William F. Raub, Deputy Assistant Secretary, Office of

Science Policy, Department of Health and Human Services (HHS). SMRCS presented NCI staff attending this meeting with a list of materials required by SMRCS from NCI to answer these questions. NCI also agreed to identify all NCI historical documents in its possession that address its Chernobyl studies and provide copies of them to SMRCS for review and analysis.

Note: On August 30-31, SMRCS support staff met with NCI headquarters staff to identify Chernobyl documents among the numerous boxes of US fallout and Chernobyl documents that had been submitted in 1998 to the Permanent Subcommittee on Investigations, Committee on Governmental Affairs, US Senate. Many thousands of pages of Chernobyl documents were identified, copied by NCI, and provided for review and annotation.

Began assembling a list of key individuals (NCI and other) associated with its Chernobyl projects–these people will be interviewed by SMRCS .

Hold SMRCS Meeting in September 1999

–Purpose: Receive briefing from NCI management and scientists on the background and current status of the NCI Chernobyl studies.

–Status: SMRCS met on September 20, and received briefings regarding management and scientific issues from Dr. Shelia Zahm, Deputy Director, Division of Cancer Epidemiology and Genetics, NCI, and other key NCI scientists. During this briefing, NCI indicated that it was holding an " International Meeting on Collaborative Chornobyl Thyroid Research Projects" on November 8-10, 1999, in Washington D.C., and that many of the key UA and BY scientists working on the thyroid studies would be present at this meeting. NCI offered to extend the meeting one day so that SMRCS would be able to take advantage of this unique opportunity to meet and interview key UA and BY staff as well as to lay the groundwork with them for the planned SMRCS site visit to UA and BY scheduled for March 2000.

Other key tasks scheduled for the previously planned November SMRCS meeting (e.g., to discuss status of document review and decide on general outline of the final report) were addressed during this September meeting.

Hold SMRCS Meeting in November 1999

–As noted above, SMRCS took advantage of the opportunity to meet and interview Ukrainian and Belarusian scientists on November 11 in lieu of this scheduled SMRCS meeting. SMRCS conducted individual interviews with the Project Directors of the UA and BY thyroid studies plus 4 senior scientists from each project. SMRCS obtained useful information on the scientific and management dynamics of the studies and made invaluable contacts for its planned site visit to UA and BY in April 2000.

Provide Briefing on the Status of the SMRCS Report to Full ACERER and the ACERER Subcommittee for Community Affairs on December 14-15, 1999

–Status: Briefing was provided by SMRCS at this meeting.

Hold SMRCS Meeting in January 2000

–Purpose: Provide briefing to and solicit input from representatives of public interest groups such as Physicians for Social Responsibility and the Alliance for Nuclear Accountability.

–Status: Combined this meeting with the February meeting noted below.

Hold SMRCS Meeting in February 2000

–Purposes: Brief and receive input form public interest groups. Review progress of preparation of draft report, describe the results of SMRCS interviews of key NCI and other US scientists.

–Status: Meeting was held on February 24. (Note: Public interest groups invited to attend this meeting were Physicians for Social Responsibility (PSR) and the Alliance for Nuclear Accountability (ANA), an "umbrella" organization that includes numerous groups with interests in radiation issues. We invited ANA to share the invitation with its member groups.) PSR was unable to be represented; public interest groups represented were ANA, the Nuclear Information and Resource Service, and the Institute for Energy and Environmental Research. SMRCS briefed these representatives and received useful input from them. After the briefing SMRCS discussed the status of report preparation and related issues.

SMRCS to Conduct Site Visit to UA and BY in March 2000

–Purposes: To meet and talk with Ukrainian and Belarusian scientists carrying out the work of the studies and to review their screening, clinical, data management, and other operations associated with the studies.

–This site visit was conducted April 11-20, 2000.

Provide Briefing to ACERER at its Scheduled April 2000 Meeting

–Purpose: To review and discuss the draft report and obtain ACERER input for final report.

–Status: This meeting was rescheduled and was held on June 7-8, The draft report was delivered to ACERER members for review on June 1, 2000 and was discussed with them on June 7.

May 2000–Deliver SMRCS Report to HHS

–Status: Because the April ACERER meeting was rescheduled to June 7-8, and the report comment period for ACERER members was extended to July 7, the date of report delivery to HHS was rescheduled to early August 2000. The report was unanimously approved by a quorum of ACERER members on August 4, 2000.

NOTE: All described ACERER and SMRCS meetings were open meetings, announced in the Federal Register

TIME LINE OF KEY EVENTS IN THE HISTORY OF THE CHERNOBYL STUDIES

1. April 26, 1986 – Chernobyl nuclear reactor explodes.

2. 1987 – Presidents Ronald Reagan and Mikhail Gorbachev agreed on the need to cooperate in the area of civilian nuclear reactor (CNR) safety.

3. 1988 – "Memorandum of Cooperation in the Field of Civilian Nuclear Reactor Safety Between the United States of America and the Union of Soviet Socialist Republics" signed by the U.S. Nuclear Regulatory Commission on behalf of the U.S. Government and the USSR State Committee for the Utilization of Atomic Energy.

4. 1990 – Under the Memorandum of Cooperation, U.S. and USSR scientists begin discussions on the feasibility and of conducting studies of thyroid disease and leukemia among USSR citizens exposed to radiation from the Chernobyl accident. National Cancer Institute (NCI) scientists are asked to participate in these discussions as individual experts, not in recognition of NCI official involvement as an Agency in these discussions.

5. 1990 – The U.S. Department of Energy (DOE) asks NCI to assume responsibility for determining the posibility of conducting thyroid disease and leukemia studies in the USSR. NCI agrees and NCI and DOE execute an Interagency Agreement (IAG) that formalized NCI's involvement in the Chernobyl studies.

6. 1991 – Breakup of USSR and the creation of the newly independent countries of Ukraine (UA) and Belarus (BY).

7. 1994 – Research protocol formalized with BY for the study of thyroid disease.

8. 1995 – Research protocol formalized with UA for the study of thyroid disease.

9. 1996 – Research protocol formalized with UA for the study of leukemia.

10. 1997 – DOE and NCI execute an IAG that for the first time clearly spells out the respective responsibilities of the two Agencies. This signals the beginning of a new era of productive cooperation between the two Agencies.

11. 1997 – NCI issues a contract to Columbia University to provide scientific, administrative, and logistics support to its Chernobyl studies.

12. 1998 – The Permanent Subcommittee on Investigations of the Subcommittee on Governmental Affairs, U. S. Senate, held a Hearing on NCI's management of its radiation studies. Concluded that NCI's Chernobyl studies suffered from delays, and lacked management oversight and openness. Recommended that the Department of Health and

Human Services (HHS) arrange for an independent review of NCI's Chernobyl studies. HHS agrees to arrange for this review.

13. 1999 – NCI reorganizes its Chernobyl studies and locates them under NCI's Division of Cancer Epidemiology and Genetics (DCEG). Dr. Gilbert Beebe named head of a new Chernobyl Research Unit in the Radiation Epidemiology Branch (headed by Dr. Elaine Ron), DCEG.

14. 1999 – HHS requests that the Federally-chartered Advisory Committee for Energy-Related Epidemiologic Research (ACERER) conduct this review. ACERER agrees and forms a subcommittee of its members, the Subcommittee for Management Review of the Chernobyl Studies, to carry out this review.

INTERAGENCY AGREEMENT
FY 1997
BETWEEN
THE DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL CANCER INSTITUTE
AND
THE DEPARTMENT OF ENERGY
OFFICE OF ENVIRONMENT, SAFETY AND HEALTH

This memorandum sets forth the terms of agreement in FY 1997 between the Department of Health and Human Services (HHS), National Cancer Institute (NCI), and the Department of Energy (DOE), Office of Environment, Safety and Health for joint implementation of the project, "U.S./Belarus/Ukraine Joint Research on the Biomedical Effects of the Chernobyl Reactor Accident."

I. DESCRIPTION OF SERVICES

This agreement is a mechanism to implement the transfer of funds to provide partial support for the Chernobyl-related leukemia and thyroid disease epidemiology studies in Ukraine and the thyroid disease epidemiology study in Belarus in fiscal year (FY) 1997 from DOE to HHS, NCI, and to define the responsibilities of each Agency with respect to these studies.

These studies will operate under the auspices of the Joint Coordinating Committee for Civilian Nuclear Reactor Safety (JCCCNRS) and applicable Binational Agreements. The total cost of these projects in FY 1997 estimated by NCI is around $2.5 million, exclusive of the cost of equipment and supplies and contributions from other agencies and/or countries.

A. DOE makes a commitment to:

Transfer at the proper time in FY 1997 agreed-upon funds to NCI to cover administrative, logistical, managerial, equipment, and supply costs incurred in the execution of activities directly related to the leukemia and thyroid disease epidemiology studies in Ukraine and the thyroid disease epidemiology study in Belarus. DOE will contribute up to $800,000 from the FY 1997 budget.

B. NCI makes a commitment to:

1. Assume all responsibility for management, coordination and oversight of the design, implementation, analysis and scientific interpretation of the results of leukemia and thyroid disease epidemiology studies of Chernobyl-exposed populations in Ukraine and Belarus.

2. Manage, coordinate and oversee the projects using staff of the NCI and/or of an NCI-funded scientific and technical support contractor.

3. Assume responsibility for all official policy, financial, management and scientific matters with the governments of Belarus and Ukraine and their relevant organizational entities and personnel.

4. Act as the sole contact point for all official project-related communications between U.S. agencies and their contractor personnel and Ukraine and Belarus Ministries and collaborating institutions and individuals. This is not intended to preclude personal scientific or technical discourse among or between scientists and physicians or limit unofficial interactions between interested parties.

5. Develop milestones on a quarterly basis for the ongoing program to be used in evaluation of the progress of the project and for authorization of payments for local support.

6. Share all reports regarding these projects with DOE and, when appropriate, with other relevant U.S. Government Agencies (Nuclear Regulatory Commission and Department of State).

7. Provide DOE with annual progress and financial reports.

8. Invite DOE observers to all review and reporting sessions.

9. Contribute financial resources from its FY 1997 budget of at least matching funds toward the implementation of the projects. (If DOE support and NCI matching funds are not sufficient to fully implement the protocols, and the remaining shortfall cannot be met from other sources, the scope of the project(s) will be revised.)

II. DURATION OF AGREEMENT

This agreement is effective when signed by both parties and shall remain in effect through the end of FY 1997 unless amended by mutual written consent of both parties. The agreement is to be renewed annually thereafter by written mutual agreement and will correspond to the Federal fiscal year. There is every intention to continue this agreement to ensure satisfactory completion of these projects.

III. PAYMENTS TO BE MADE TO: NATIONAL CANCER INSTITUTE

Reimbursement by Standard Form 1080 or 1081 or Treasury Online Payment and Costing (OPAC) system.

Submit billing to:

FINANCE DIVISION
P.O. BOX 2001
OAK RIDGE, TN 37831

IV. REIMBURSING AGENCY CODE: DE-A105-92EH89188.000

This agreement will operate under the following NCI codes:

Agreement Number:	Y3-CB-0020
Appropriation:	7570849
Common Account Number:	7-8422517

V. LEGAL AUTHORITY

The legal authority for NCI to enter into this agreement is encompassed within the provisions of the Economy Act of 1932 as amended (31 U.S.C. 1535 and 1536).

VI. TRAVEL

Travel under this agreement is subject to allowances authorized in accordance with the Federal Travel Regulations, Joint Federal Travel Regulations, and/or Foreign Services Regulations.

VII. EQUIPMENT

Any equipment procured shall not be required to be returned to DOE or NCI.

VIII. PROJECT OFFICERS

NCI: IHOR J. MASNYK, Ph.D.
Radiation Effects Branch
National Cancer Institute
EPN, Suite 530
Bethesda, MD 20892-7391
Tel: (301) 496-9326
Fax: (301) 496-1224
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DOE: BARRETT N. FOUNTOS
U.S. Department of Energy
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EH-63/270CC
19901 Germantown Road
Germantown, MD 20874-1290
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Fax: (301) 903-1413
e-mail: barrett.fountos@eh.doe.gov

IX. MODIFICATIONS OR CANCELLATIONS

This agreement, or any part of its specific provisions, may be revised by signature approval of both parties signatory hereto. Cancellation of the agreement may be accomplished only at the expiration of 90-day advanced notification by either party.

X. RIGHTS IN DATA

NCI may:

1. Establish a claim to copyright scientific or technical articles based on, or containing, data first produced in the performance of this agreement.

2. Use, release to others, reproduce, or publish any data first produced in the performance of this agreement, provided that a copy of the final document is provided to DOE.

STATEMENT OF WORK SUMMARY

DOE will provide a portion of the funds required (up to $800,000) for the performance of specified activities in support of the three projects (U.S.-Belarus Thyroid, U.S.-Ukraine Thyroid, U.S.-Ukraine Leukemia) in FY 1997. NCI will contribute at least matching funds to carry out these three projects.

In addition, NCI (Radiation Effects Branch), in consultation with Binational Advisory Groups and working groups of experts, tailored to specific technical requirements, will assume full responsibility for design, implementation, analysis and scientific interpretation of leukemia and thyroid disease epidemiologic studies of Chernobyl-exposed populations in Belarus and Ukraine; manage, coordinate and oversee all ongoing activities; assume responsibility for all official policy, management issues, and all financial matters; be the sole source of all official contacts for project-related communications between all participating entities: U.S. Agencies, contractors, advisors, consultants, and Belarus and Ukrainian organizations and personnel. This is not intended to preclude personal scientific or technical discourse among or between scientists and physicians or limit unofficial interactions between interested parties.

NCI will provide DOE copies of all reports, minutes of meetings, and other documentation related to these studies and will provide DOE an annual progress/financial report within 30 days of the end of the fiscal year. NCI will invite DOE staff as observers to program reporting sessions.

NATIONAL CANCER INSTITUTE

Richard J. Klausner, M.D., Director
National Cancer Institute
Department of Health and Human Services

Date: DEC 23 1996

DEPARTMENT OF ENERGY

Tara O'Toole, M.D., M.P.H.
Assistant Secretary for Environment,
Safety and Health
Department of Energy

Date: 12/19/96

FRETTERS MEMBERSHIP

NAME	AFFILIATION
Dr. Lynn Anspaugh	Lawrence Livermore National Laboratory
Dr. David Becker	The New York Hospital-Cornell Medical Center
Dr. Gilbert Beebe	National Cancer Institute
Dr. Andre Bouville	National Cancer Institute
Dr. Bertrand Brill	University of Massachusetts Medical Center
Dr. Jacob Robbins	National Institute of Diabetes and Digestive and Kidney Diseases, NIH
Dr. Roy E. Shore	New York University Medical Center
Dr. Lester Van Middlesworth	University of Tennessee at Memphis
Dr. Bruce Wachholz	National Cancer Institute
Dr. Jan Wolff	National Institute of Diabetes and Digestive and Kidney Diseases, NIH